UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,299	10/09/2001	Yoshiya Gunji	212289US0PCT	4922

38108 7590 09/16/2005

CERMAK & KENEALY LLP
ACS LLC
515 EAST BRADDOCK ROAD
SUITE B
ALEXANDRIA, VA 22314

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,299	GUNJI ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,7-10 and 12-31* is/are pending in the application.

4a) Of the above claim(s) *14,15,18,19 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,7-10,12,13,16,17,20,21 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] Claims 1-2, 5, 7-10, and 12-31 are pending in the application.

[3] Applicants' amendment to the claims, filed on 6/24/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Applicants' arguments filed 6/24/2005 have been fully considered and are deemed to be persuasive to overcome some of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

[6] Claims 14-15, 18-19, and 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/14/2004.

[7] Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are being examined on the merits.

Information Disclosure Statement

[8] Applicants note the references cited in the IDS filed on 4/6/2004 have not been considered by the examiner. In response, the examiner has considered EP 0435132 but has not considered the Office action from the Chinese Patent Office. Form PTO-1449 lists the Office action by the Chinese Patent Office as a foreign patent document, however, this is not a foreign patent document. A copy of Form PTO-1449 is attached to the instant Office action.

Claim Objections

[9] Claim 17 recites the improper alternative expression "selected from a group consisting of" and should be replaced with, for example, "selected from the group consisting of."

Claim Rejections - 35 USC § 112, Second Paragraph

[10] The rejection of claims 1-2, 5, 7-10, 12-13, and 26-31 as being unclear in the recitation of "hybridizes" and as being indefinite in that the claims fail to indicate a length of time of hybridization is maintained the reasons of record and the reasons stated below. In view of applicants' amendment, claims 17 and 21 are included in the instant rejection.

RESPONSE TO ARGUMENT: Applicants argue: 1) the recitation of hybridization time is an unnecessary limitation as it depends upon which buffer is utilized and

depending on the chosen buffer, one of skill in the art can choose an appropriate length of time and 2) Southern hybridization including a washing step is within the ability of a skilled artisan.

Applicants' argument is not found persuasive. It is noted that the independent claims specifically recite a buffer to be used in the hybridization, *i.e.,* "a salt solution of 1xSSC and 0.1%SDS." SSC is an art-recognized buffer whose composition is well known – see, *e.g.,* p. 10 of "Current Protocols in Molecular Biology" as cited in the Office action mailed 3/24/2005. Thus, a skilled artisan would recognize that a specific buffer *is* recited in the claims. Further, as noted in the previous Office action, the length of time of hybridization has a significant effect on the hybridization reaction, which is undisputed by applicants. In view of the failure of the claims to recite a length of time of hybridization, it is unclear as to applicants' intended time of hybridization. Is the intended time of hybridization at 1 second, 1 minute, 1 hour, etc.? Consequently, it is unclear as to the scope of dihydropicolinate synthase or aspartokinase polypeptides that are encompassed by the claims. It is suggested that applicants identify the intended length of time of the hybridization reaction.

Claim Rejections - 35 USC § 112, First Paragraph

[11] The written description rejection of claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Initially, it is noted that a substantial portion of applicants' arguments addressing the instant written description rejection appear to be directed to the "undue experimentation" required to make and use the claimed invention. However, this is not the issue at hand. Instead, the issue is whether the specification adequately describes the claimed invention. To the extent applicants' arguments apply to the written description rejection, the arguments are addressed below.

Also, it is noted that in view of the failure of the claims to recite a particular length of time of hybridization, the scope of the recited nucleic acids is unclear. In accordance with MPEP 2111, the examiner has interpreted claims 1b), the first occurrence of part b) in claim 5, and 21b) as encompassing any nucleic acid that encodes a protein with dihydrodipicolinate synthase activity and the examiner has interpreted the second occurrence of part b) of claim 5 and claims 7b), and 17b) as encompassing any nucleic acid that encodes a protein with aspartokinase activity. Also, in view of the recitation of "a nucleotide sequence" rather than "the nucleotide sequence," the examiner has interpreted claims 17(a) and 21(e), which recite "comprising *a* nucleotide sequence of the nucleotide numbers..." as encompassing any nucleic acid encoding a protein having aspartokinase or dihydrodipicolinate synthase activity, respectively.

Applicants argue: 1) in view of a previous amendment to limit the claims to the strain of *Methylophilus methylotrophus,* the genus of claimed *M. methylotrophus* bacteria having enhanced dihydrodipicolinate synthase activity are fully described and 2) the genes and proteins having enhanced activity are known in the art and a skilled

artisan can make all members of the claimed genus of *M. methylotrophus* bacteria having enhanced dihydrodipicolinate synthase activity. Applicants point to Appendices A and B in support of their arguments.

Applicants' arguments are not found persuasive. The examiner acknowledges the previous amendment to limit the strain as recited in claims 1-2, 5, 7-10, 12-13, and 26-31 to an *M. methylotrophus* bacterium. However, the examiner maintains the position that the specification fails to describe all members of the genus of claimed *M. methylotrophus* bacteria. In this case, the genus of recited *M. methylotrophus* bacteria of claims 1-2, 5, 7-10, 12-13, and 26-31 encompasses species that have enhanced dihydrodipicolinate synthase activity and/or enhanced aspartokinase activity and optionally with enhanced activities of the enzymes recited in claims 8, 10, 26, or 27 by *any* conceivable method. In this case, the specification discloses only a single representative species of the *M. methylotrophus* bacteria of claim 1, *i.e.,* a *M. methylotrophus* host cell transformed with an expression vector encoding SEQ ID NO:10, the specification discloses only a single representative species of the genus of *M. methylotrophus* bacteria of claim 5, *i.e.,* a *M. methylotrophus* host cell transformed with an expression vector or vectors encoding SEQ ID NO:6 and 10, the specification discloses only a single representative species of the genus of *M. methylotrophus* bacteria of claim 7, *i.e.,* a *M. methylotrophus* host cell transformed with an expression vector encoding SEQ ID NO:6, the specification discloses only a single representative species of the genus of DNAs of 16-17, *i.e.,* a DNA encoding SEQ ID NO:6, and the specification discloses only a single representative species of the genus of DNAs of

claims 20-21, *i.e.,* a DNA encoding SEQ ID NO:10. Other than these representative species, the specification fails to describe any other additional representative species, which is undisputed by applicants. Also undisputed by applicants is that the genus of claimed or recited *M. methylotrophus* bacteria or DNAs encompasses species that are widely variant. For the genus of claimed or recited *M. methylotrophus* bacteria, it should be noted that the genus encompasses species that are widely variant with respect to: 1) the method of enhancing dihydrodipicolinate synthase activity and/or enhanced aspartokinase activity and 2) the sequences of the variants of SEQ ID NO:5 and 9. For the genus of claimed DNAs, the genus is widely variant with respect to the sequences of the variants of SEQ ID NO:5 and 9. Contrary to applicants' argument that the "genes and proteins having enhanced activity are...known in the art," the variants of SEQ ID NO:5 and/or 9 are not necessarily "known in the art." In this case, there is wide variation among the members of the genus and consequently, the disclosed representative species are not representative of the *entire* genus, as evidenced by MPEP § 2163, which states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." Apparently, applicants point to Appendices A and B as showing that the invention is not "in an unpredictable art." However, even in view of the evidence of Appendices A and B there is no way to visualize or recognize *a priori* the structures of those variants of SEQ ID NO:5 and/or 9 as encompassed by the claims that would maintain the desired activity. Consequently, the specification, by disclosing only a single representative species of each genus as described above, fails to describe

all members of the claimed or recited genus of *M. methylotrophus* bacteria or DNAs, which encompasses widely variant species.

[12] The scope of enablement rejection of claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue that in view of the evidence presented in Appendices A and B, it would not require undue experimentation for a skilled artisan to make all *M. methylotrophus* bacteria and DNAs encompassed by the claims.

Applicants' argument is not found persuasive. Initially, it is noted that in view of the failure of the claims to recite a particular length of time of hybridization, the scope of the recited nucleic acids is unclear. In accordance with MPEP 2111, the examiner has interpreted claims 1b), the first occurrence of part b) in claim 5, and 21b) as encompassing any nucleic acid that encodes a protein with dihydrodipicolinate synthase activity and the examiner has interpreted the second occurrence of part b) of claim 5 and claims 7b), and 17b) as encompassing any nucleic acid that encodes a protein with aspartokinase activity. Further, in view of the recitation of "a nucleotide sequence" rather than "the nucleotide sequence," the examiner has interpreted claims 17(a) and 21(e), which recite "comprising *a* nucleotide sequence of the nucleotide numbers..." as encompassing any nucleic acid encoding a protein having aspartokinase or dihydrodipicolinate synthase activity, respectively.

It is noted that applicants do not dispute the examiner's assertion that the scope of *M. methylotrophus* bacteria encompasses those that are modified to enhance dihydrodipicolinate synthase and/or aspartokinase activity by any conceivable method. Further, applicants' arguments do not address these methods of enhancement. Instead, applicants' arguments address only the scope of nucleic acids encoding the proteins having dihydrodipicolinate synthase and/or aspartokinase activity.

In this case, as noted above, the claims drawn to *M. methylotrophus* bacteria are so broad as to encompass all *M. methylotrophus* bacteria having any modification such that the activity of any polypeptide that has dihydrodipicolinate synthase and/or aspartokinase activity and optionally the activity of those enzymes recited in claims 8, 10, 26 or 27 is enhanced by any conceivable method. The claims drawn to DNAs are so broad as to encompass DNAs encoding any protein having dihydrodipicolinate synthase and/or aspartokinase activity. The guidance and working examples as provided by the specification is not sufficient to enable the full scope of recited *M. methylotrophus* bacteria and DNAs. In this case, the specification discloses only the following working examples of the claimed or recited *M. methylotrophus* bacteria and DNAs: a *M. methylotrophus* host cell transformed with an expression vector encoding SEQ ID NO:10, a *M. methylotrophus* host cell transformed with an expression vector or vectors encoding SEQ ID NO:6 and 10, a *M. methylotrophus* host cell transformed with an expression vector encoding SEQ ID NO:6, a DNA encoding SEQ ID NO:6, and a DNA encoding SEQ ID NO:10. While applicants argue that the alignments shown in Appendices A and B would reveal those residues that can or cannot be altered with an

expectation of maintaining the desired activity, it is not clear to the examiner that the sequences used in the alignments were available to a skilled artisan at the earliest effective filing date of the invention, *i.e.,* April 9, 1999. That the sequences were available at the time of filing is important as the specification and prior art must enable the claimed invention at the time of filing. Even assuming *arguendo* the sequences were available at the time of the invention, these alignments fail to teach a skilled artisan how to make any nucleic acid that encodes a polypeptide having dihydrodipicolinate synthase and/or aspartokinase activity as broadly encompassed by the claims. As noted in the previous Office action, the effects of altering an encoding nucleic acid on the function of the encoded polypeptide are highly unpredictable, which is evidenced by Branden et al. and Witkowski et al. and is undisputed by applicants. In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of trial-and-error experimentation that is required, the examiner maintains the position that undue experimentation is required for a skilled artisan to make the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

[13] The rejection of claims 16-17 and 20-21 under 35 U.S.C. 102(b) as being anticipated by Kojima et al. (WO 95/16042; cited in the IDS filed 9/5/2003) is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the amino acid sequences of the dihydrodipicolinate synthase and aspartokinase polypeptides of Kojima et al. differ from SEQ ID NO:10 and 6, respectively, in "more than 'several' amino acids," referring to p. 34, lines 3-6 of the specification as defining the term "several."

Applicants' argument is not found persuasive. Regarding the term "several," it is noted that applicants' cited "definition" merely provides an exemplary number of amino acids that is encompassed by the term "several." This "definition" fails to provide a specific number of amino acids alterations. In this case, the examiner has broadly interpreted the term "several" to mean an unlimited number of amino acid alterations. Also, regarding claims 17 and 21, in view of the failure of the claims to recite a particular length of time of hybridization, the scope of the recited nucleic acids is unclear. In accordance with MPEP 2111, the examiner has interpreted claim 21 parts (e) and (f) as encompassing any nucleic acid that encodes a protein with dihydrodipicolinate synthase activity and the examiner has interpreted claim 17 parts (a) and (b) as encompassing any nucleic acid that encodes a protein with aspartokinase activity. In view of these broad, but reasonable interpretations, the reference of Kojima et al. anticipates the claims.

Conclusion

[14] Status of the claims:

Claims 1-2, 5, 7-10, and 12-31 are pending.

Claims 14-15, 18-19, and 22-25 are withdrawn from consideration.

Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 are rejected.

No claim is in condition for allowance.

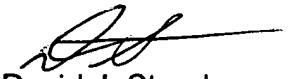
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs and alternate Fri, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656